CLAIMS

What we claim is:

1. A double-stranded short interfering nucleic acid (siNA) molecule that inhibits replication of a hepatitis C virus (HCV), wherein one of the strands of said double-stranded siNA molecule is an antisense strand which comprises a nucleotide sequence that is complementary to the nucleotide sequence of an HCV RNA or a portion thereof and the other strand is a sense strand which comprises a nucleotide sequence that is complementary to the nucleotide sequence of the antisense strand, and wherein a majority of the pyrimidine nucleotides present in said double-stranded siNA molecule comprises a sugar modification.

2. The siNA molecule of claim 1, wherein the HCV RNA comprises HCV minus strand RNA.

3. The siNA molecule of claim 1, wherein the HCV RNA comprises HCV plus strand RNA.

4. The siNA molecule of claim 1, wherein the siNA molecule comprises no ribonucleotides.

5. The siNA molecule of claim 1, wherein the siNA molecule comprises ribonucleotides.

6. The siNA molecule of claim 1, wherein all the pyrmidine nucleotides in the siNA molecule comprise sugar modifications.

7. The siNA molecule of claim 6, wherein the modified pyrimidine nucleotides are selected from 2'-deoxy-pyrimidine, 2'-O-alkyl pyrimidine, 2'-C-alkyl pyrimidine, 2'-deoxy-2'-fluoro-pyrimidine, 2'-amino pyrimidine, 2'-methoxy-ethoxy pyrimidine, and 2′-O, 4′-C-methylene pyrimidine nucleotides, alone or in any combination thereof.

8. The siNA molecule of claim 7, wherein the 2'-O-alkyl primidine nucleotide is 2'-O-methyl or 2'-O-allyl.

9. The siNA molecule of claim 1, wherein the nucleotide sequence of the antisense strand of the double-stranded siNA molecule is complementary to an RNA encoding an HCV protein or a fragment thereof.

10. The siNA molecule of claim 1, wherein each strand of the siNA molecule comprises about 19 to about 29 nucleotides, and wherein each strand comprises at least about 19 nucleotides that are complementary to the nucleotides of the other strand.

11. The siNA molecule of claim 1, wherein said siNA molecule is assembled from two oligonucleotide fragments, wherein one fragment comprises the nucleotide sequence of the antisense strand of the siNA molecule and the second fragment comprises the nucleotide sequence of the sense strand of the siNA molecule.

12. The siNA molecule of claim 1, wherein the sense strand is connected to the antisense strand via a linker molecule.

13. The siNA molecule of claim 12, wherein said linker molecule is a polynucleotide linker.

14. The siNA molecule of claim 12, wherein said linker molecule is a non-nucleotide linker.

15. The siNA molecule of claim 1, wherein any pyrimidine nucleotides present in the sense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides and wherein any purine nucleotides present in the sense region are 2'-deoxy purine nucleotides.

16. The siNA molecule of claim 1, wherein the sense strand comprises a 3'-end and a 5'-end, and wherein a terminal cap moiety is present at the 5'-end, the 3'-end, or both of the 5' and 3' ends of said sense strand.

17. The siNA molecule of claim 16, wherein said terminal cap moiety is an inverted deoxy abasic moiety.

18. The siNA molecule of claim 1, wherein the antisense strand comprises one or more 2'-deoxy-2'-fluoro pyrimidine nucleotides and one or more 2'-O-methyl purine nucleotides.

19. The siNA molecule of claim 1, wherein any pyrimidine nucleotides present in the antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides and wherein any purine nucleotides present in the antisense strand are 2'-O-methyl purine nucleotides.

20. The siNA molecule of claim 1, wherein the antisense strand comprises a phosphorothioate internucleotide linkage at the 3' end of said antisense strand.

21. The siNA molecule of claim 1, wherein the antisense strand comprises a glyceryl modification at the 3' end of said antisense strand.

22. The siNA molecule of claim 1, wherein each strand of the siNA molecule comprises 21 nucleotides.

23. The siNA molecule of claim 22, wherein about 19 nucleotides of each strand of the siNA molecule are base-paired to the complementary nucleotides of the other strand of the siNA molecule and wherein at least two 3' terminal nucleotides of each strand of the siNA molecule are not base-paired to the nucleotides of the other strand of the siNA molecule.

24. The siNA molecule of claim 23, wherein each of the two 3' terminal nucleotides of each fragment of the siNA molecule are 2'-deoxy-pyrimidines.

25. The siNA molecule of claim 24, wherein the 2'-deoxy-pyrimidine is 2'-deoxy-thymidine.

26. The siNA molecule of claim 22, wherein 21 nucleotides of each strand of the siNA molecule are base-paired to the complementary nucleotides of the other strand of the siNA molecule.

27. The siNA molecule of claim 22, wherein about 19 nucleotides of the antisense strand are base-paired to the nucleotide sequence of an HCV RNA or a portion thereof.

28. The siNA molecule of claim 22, wherein 21 nucleotides of the antisense strand are base-paired to the nucleotide sequence of an HCV RNA or a portion thereof.

29. The siNA molecule of claim 1, wherein the 5'-end of the antisense strand optionally includes a phosphate group.

30. The siNA molecule of claim 1, wherein the nucleotide sequence of the antisense strand or a portion thereof is complementary to the nucleotide sequence of the 5'-untranslated region of an HCV RNA or a portion thereof.

31. The siNA molecule of claim 1, wherein the nucleotide sequence of the antisense strand or a portion thereof is complementary to the nucleotide sequence of an HCV RNA or a portion thereof that is present in the RNA of at least fifteen HCV isolates.

32. A pharmaceutical composition comprising the siNA molecule of claim 1 in an acceptable carrier or diluent.

33. A medicament comprising the siNA molecule of claim 1.

34. An active ingredient comprising the siNA molecule of claim 1.

35. The use of a double-stranded short interfering nucleic acid (siNA) molecule that inhibits replication of a hepatitis C virus (HCV), wherein one of the strands of the double-stranded siNA molecule is an antisense strand which comprises a nucleotide sequence that is complementary to the nucleotide sequence of an HCV RNA or a portion thereof and the other strand is a sense strand which comprises a nucleotide sequence that is complementary to the nucleotide sequence of the antisense strand, and wherein a majority of the pyrimidine nucleotides present in the double-stranded siNA molecule comprises a sugar modification.